

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

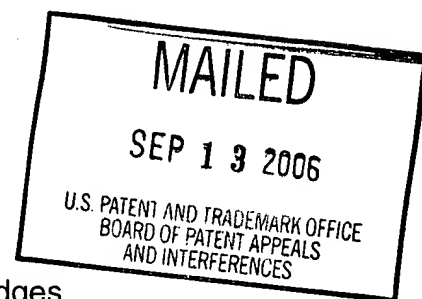
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte FRANCIS V. CHISARI, and ANDREAS CERNY

Appeal No. 2006-0211
Application No. 08/854,825

ON BRIEF



Before MILLS, GRIMES, and LEOVITZ, Administrative Patent Judges.

LEOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to polypeptides that induce an immunological response to hepatitis C virus, and methods of using the polypeptides. The examiner has rejected the claims as lacking written description. We have jurisdiction under 35 U.S.C. § 134. We reverse.

Background

Hepatitis C virus ("HCV") is one of the major causes of liver disease, including chronic hepatitis and hepatocellular cancer. Specification, page 1, lines 15-25; page 2, lines 13-16. The genome of HCV has been completely sequenced and is known to encode a large polyprotein containing 3011 amino acids that is processed into several

different proteins. Id., page 1, lines 26-34. The application describes the identification of specific peptide fragments (e.g., 9-10 amino acids in length and having a defined sequence) within the polyprotein which are able to elicit an immunological cell-mediated response to HCV. Id., page 6, lines 15-35; page 44, line 5-page 46, line 25. Under normal conditions, when a virus infects a host cell, the infected cell may process the viral proteins into smaller antigenic peptide fragments. Id., page 4, lines 7-24. The peptide fragments become associated with HLA molecules (HLA-peptide complex), which are transported to the cell surface. Id., page 4, lines 24-28. At the cell surface, the peptide fragment in the context of the HLA molecule is specifically recognized by T-cell receptors present on the surface of cytotoxic T-cells ("CTL"). Id., page 4, lines 28-36. Binding of the HLA-peptide complex to the CTL T-cell receptor activates the T-cell, initiating a T-cell response to eliminate viral-infected cells. Id., page 3, lines 17-31. Brief, page 2. Each of the peptide fragments is referred to as a "CTL epitope."

Discussion

Representative claim

Claims 67-97 are on appeal. We selected claim 67 as representative. It reads as follows:

67. An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that

(a) has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is

LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2),
QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO:3),
KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), or

LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is

ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1),
LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), or
SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),

wherein said molecule comprises at least eight amino acids and less than 50 amino acids,

with the provisos that (i) when said selected CTL epitope is SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), then said molecule comprises from at least eight amino acids to less than 25 amino acids, or (ii) when said selected CTL epitope is LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2) then said molecule comprises at most ten amino acids.

Claim 97 is the same as claim 67, but contains the additional limitation that the “CTL epitope maintains an XaaLeuXaaXaaXaaXaaXaaXaaVal or XaaLeuXaaXaaXaaXaaXaaXaaXaaVal motif.” In this specification, this motif is described as being necessary for the peptide to bind to the MHC complex, HLA-A2.1. Specification, page 44, lines 9-15.

Written description, 35 U.S.C. § 112, first paragraph

Claims 67-97 stand rejection under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification. Relying on University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the examiner stated: “The claims encompass a large genus of peptides that can carry substitutions, insertions, and/or deletions. The specification does not describe the synthesis, isolation, and characterization of a single mutant peptide. The specification

does not teach which amino acids within any given epitope can tolerate modifications.” Answer, page 6. The examiner also described four specific deficiencies in the claimed subject matter, and cited scientific publications to support his arguments. Id., page 6.

Appellant’s only rebuttal in this appeal to the examiner’s rejection was that “the claims here at issue are framed in definite, structural formulas” that “simply cannot be brought within the rubric of Lilly¹.” Brief, page 5.

Contrary to Appellant’s argument, we find that University of California v. Eli Lilly & Co. (“Lilly”), 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) is applicable to the facts of this case. In the Lilly case, only a single cDNA to rat insulin was described in the patent specification, but the Patentee had claims that covered broader genera of cDNAs, coding for mammalian and vertebrate insulins, respectively. Lilly, 119 F.3d at 1563, 1567, 43 USPQ2d at 1401, 1405. In an infringement suit, the validity of these claims was challenged. The court held the claims invalid for failing to provide an adequate written description of the claimed genus.

In claims to genetic material, however, a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA,” without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id., 119 F.3d at 1568, 43 USPQ2d at 1406.

The Lilly court found the claims invalid for lack of written description for at least two reasons: because the patent lacked a definition of other species members that fell

¹ University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)

within the genus, and for its failure to describe structural features “commonly possessed” by the genus members. After carefully reviewing the specification and claims at issue in this appeal, we do not find these deficiencies to be present here. Thus, we will reverse the examiner, but not for the reasons argued in Appellants’ Brief.

As required by Lilly, claim 67 provides a definition of members of the claimed genus. Definite structural formulae are recited in claim 67 of seven reference sequences of nine or ten amino acids (e.g., “LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2)”) that are required by the claim preamble to induce an HCV-specific response in cytotoxic T lymphocytes. Each reference sequence can be modified by one or two amino acid substitutions, deletions or insertions, only a modest degree of variation that requires the presence of at least about 80% (8/10) or 78% (7/9) of the recited amino acids. The specification also provides general guidance on amino acid substitutions and modifications that can be made to it. Specification, page 11, line 9-15; page 13, line 27-Page 14, line 13; page 15, line 3-36. Using this information, specific species within the genus can be written down. In addition, natural variations of the reference sequence are mentioned, including an example of an amino acid substitution. Id., Pages 56-57. Taken together, the facts indicate that not only did Appellants possess each single reference sequence, but also had a picture of individual species that fell within the claimed genus.

Furthermore, we find that the specification describes a structural feature that is “commonly possessed” by members of the genus. Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. On page 44, line 12, the specification identifies the HLA-A2.1 binding motif

that is characteristic ("commonly possessed") of peptides having the ability to induce an immune response. All but one of the claimed reference sequences possess this motif.

In sum, we do not see any difficulty in recognizing the genus of peptides recited in claim 67.

Appellant asserted Lilly was inapplicable because the claims at issue were more like those described for a chemical formula. In such cases, the court had stated:

... generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.

Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

The type of claim referred to in Lilly is a generic formula comprising a skeletal chemical structure that exactly specifies the positions in the skeleton where chemical substitutions can be made, and of what type. Claim 67 does not have this rigid specification because it does not describe at what position in the reference sequence amino acid modifications can be made. For this reason, we do not agree with Appellant that Lilly's discussion of generic formula is dispositive for this case.

The examiner has the initial burden of presenting by evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). This burden has not been met. No evidence has been provided that the claimed genus, which varies by no more than one or two amino acids from a reference sequence, is so imprecise that a defined structure could not be imagined by one skilled in the art. The failure in Lilly, according to the court, was the lack of a description of

how the single disclosed species (from a rat) defined other members of the claimed genus. But, here the facts are different. The claims contain a definite statement about the genus: variations of 1 or 2 amino acids in a reference sequence. Specific members of the genus can be written out.

The examiner's concern seems to be that the application does not specify which amino acids in the claimed motif are necessary for the peptide to retain its claimed activity in stimulating an HCV response in cytotoxic lymphocytes. Answer, page 6.

We do not understand § 112, first paragraph, to impose the strict requirement that a specification describe "critical residues for activity" in order to be a valid claim. In another leading case on the written description requirement for genetic materials, Enzo Biochem. Inc. v. Gen-Probe Inc. ("Enzo"), 323 F.3d 956, 964, 967, 63 USPQ2d 1609, 1613, 1615 (Fed. Cir. 2002), the court adopted standards set forth by the PTO in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001), as well as an example provided in accompanying materials (Synopsis of Application of Written Description Guidelines, Example 9, at 35-37) in which the PTO determined that genus claims to nucleic acids based on their hybridization properties and functional properties were adequately described. No critical residues in this example were disclosed, yet they were considered by the Enzo court to be in compliance with the statute. We do not see any reason to treat the claims at issue any differently.

In stating his position, the examiner relied upon several publications² to show

² Representative of these are: Bertolotti et al., J. Exp. Med., Vol. 180, pp.933-943, 1994; Nayersina et al., J. Immunol., Vol. 150, pp. 4659-4671, 1993; Johnson et al., J. Exp. Med., Vol. 175, pp.961-971, 1992.

that single amino acid changes can have dramatic effects on the CTL activity of peptides. Answer, page 6. While we commend the examiner's diligence in articulating and supporting his position, we do not find these facts fatal to the claims at issue.

We agree that the cited publications establish that not every amino acid change would be expected to produce a peptide with the claimed CTL activity. From this, the examiner reached the conclusion that since Appellant doesn't know the positions in the reference sequence where modifications would affect (e.g., abolish) its activity, Appellant hasn't described its structure.

"Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter." Capon v. Eshhar, 418 F.3d 1349, 1359, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005). The evidence of record establishes that the knowledge and maturity of the prior art as it related to cytotoxic lymphocyte activity was particularly advanced by the filing date of the instant application. The specification provides a discussion in its "Background" section of what was known about the CTL response, including characteristics of CTL epitopes and how they are presented to T-cells. Specification, page 3, line 17-page 4, line 36. The publications cited by the examiner (see, footnote 2) establish that CTL epitopes had been identified for other viruses and that scientists were adept at manipulating them (including by making amino acid substitutions) to determine how structure affected their ability to activate T-cells. The examiner took the position that the "glass was half empty" and therefore

incomplete, rather than evaluating the other half that filled it. We find that the state of the art had developed to such a mature extent that the disclosure of a reference sequence, a definition of how much amino acid modification is encompassed, and a recitation of a functional activity is sufficient to provide a written description of the claimed subject matter. For these reasons which are independent of our Lilly analysis, we find that the examiner has failed establish to that the claims lack a written description.

“[I]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See In re Angstadt, 537 F.2d 498, 504 (CCPA 1976).” Capon, 418 F.3d at 1359, 76 USPQ2d at 1085 (Fed. Cir. 2005). In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976), involved a claim to a process of catalytic oxidation of alkylaromatic hydrocarbons utilizing a catalyst having a generic formula. The Board had affirmed a rejection under § 112, first paragraph, for not providing an enabling disclosure. The dispute centered on the breadth of the catalyst (“Claim 27 literally reads on thousands of metal salt complexes in which the metal salt moiety may comprise any one of at least 50 metal cations combined with any inorganic anion.” Angstadt, 537 F.2d at 502, 190 USPQ at 218 (fn.2)), and whether the specification provided a sufficient number of examples of catalysts to enable the full scope of the claimed process. Evidently, the specification did not describe enough about the structure of the recited catalysts to allow the skilled worker to know, without

additional experimentation, whether a catalyst in the scope of the claim would work in the claimed process. This is the same deficiency which now bothers the examiner in the instant appeal. The court in Angstadt concluded that, even in an unpredictable art, a disclosure of every effective species was not required. Angstadt, 537 F.2d at 502, 190 USPQ at 218.

For the reasons as discussed above, this rejection is reversed.

Summary

The rejection of claims 67-97 under § 112, first paragraph, is reversed.

REVERSED


Demetra J. Mills
Administrative Patent Judge


Eric Grimes
Administrative Patent Judge


Richard Lebovitz
Administrative Patent Judge

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